ANTI-SARS-COV-2 ANTIBODIES AND USES THEREOF

CROSS REFERENCE

[0001] This application claims the priorities of Foreign Applications No. CN202010203065.1, filed on Mar. 20, 2020; PCT/CN2020/080532, filed Mar. 21, 2020; PCT/CN2020/084097, filed on Apr. 10, 2020; PCT/CN2020/084805, filed on Apr. 14, 2020; and PCT/CN2020/108718, filed on Aug. 12, 2020; which are hereby incorporated by reference.

FIELD OF THE DISCLOSURE

[0002] The present disclosure generally relates to novel anti-SARS-COV-2 antibodies, pharmaceutical composition containing the same and the use thereof.

BACKGROUND

[0003] The recent outbreak of the new coronavirus, SARS-CoV-2 poses a serious global health emergency. SARS-CoV-2 is a positive-sense single-stranded RNA (+ssRNA) virus which belongs to the betacoronavirus family and shares substantial genetic and functional similarity with other pathogenic human betacoronaviruses, including Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV, also called SARS-CoV-1) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Like other coronaviruses, SARS-CoV-2 has four structural proteins, known as the S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins; the S, E, and M proteins together create the viral envelope; inside the envelope is the N protein bounding to the RNA genome (~30 kb) in a continuous beads-on-a-string type conformation.

[0004] The spike protein is the protein responsible for allowing the SARS-CoV-2 virus to attach to the membrane of a host cell, the receptor binding domain (RBD) of the spike protein of SARS-CoV-2 recognizes and attaches to the angiotensin-converting enzyme 2 (ACE2) receptor of host cells to use them as a mechanism of cell entry. The overall ACE2-binding mechanism is virtually the same between SARS-CoV-2 RBD and SARS-CoV RBD, indicating convergent ACE2-binding evolution between these two viruses. This suggests that disruption of the RBD and ACE2 interaction would block the entry of SARS-CoV-2 into the target cell. Indeed, a few such disruptive agents targeted to ACE2 have been shown to inhibit SARS-CoV infection. However, given the important physiological roles of ACE2 in vivo, these agents may have undesired side effects. Anti-RBD antibodies, on the other hand, are therefore more favorable. Furthermore, SARS-CoV-RBD or MERS-CoV RBD-based vaccine studies in experimental animals have also shown strong polyclonal antibody responses that inhibit viral entry. Such critical proof-of-concept findings indicate that anti-RBD antibodies might effectively block SARS-CoV-2 entry.

[0005] No SARS-CoV-2-specific treatments or vaccine are currently available, and the currently existing detective measures for SARS-CoV-2 infection are time-consuming and insensitive. Hence, there is an urgent need for novel anti-SARS-CoV-2 antibodies.

BRIEF SUMMARY OF THE INVENTION

[0006] In one aspect, the present disclosure is directed to a modified antibody or an antigen-binding fragment thereof comprising at least an antigen-binding domain having an antigen-binding affinity and a covalently linked modified human IgG constant domain, wherein the antigen-binding affinity comprises SARS-CoV-2 binding affinity, the antigen-binding affinity comprises at least 50% less or non-detectable binding affinity to SARS-CoV or MERS-CoV compared to the SARS-CoV-2 binding affinity, and wherein the modified human IgG constant domain comprises a substitution with tyrosine at amino acid residue 252, a substitution with threonine at amino acid residue 254, and a substitution with glutamic acid at amino acid residue 256, numbered according to the EU index as in Kabat, the modified antibody has an increased affinity for FcRn compared to the affinity to FcRn of an antibody having a wild type human IgG constant domain.

[0007] In another aspect, the present disclosure is directed to a pharmaceutical composition comprising at least one the modified antibody or an antigen-binding fragment thereof of disclosed herein, at least one nucleic acid encoding the modified antibody or the antigen-binding fragment thereof, or a combination thereof, and one or more pharmaceutically acceptable carriers.

[0008] In another aspect, the present disclosure is directed to a method for treating or preventing a disease in a subject in need thereof, the method comprising administering an effective dosage of any of the pharmaceutical composition of disclosed herein to the subject;

[0009] wherein the pharmaceutical composition is configured to be administered to the subject to maintain a plasma concentration of the modified antibody or an antigen-binding fragment thereof in a therapeutic effective range of from 10 μg/mL to 3500 μg/mL for a time period in a range of from 1 day to 12 months after administering the pharmaceutical composition; and

[0010] wherein the subject is infected with, exhibiting one or more symptoms of being infected with, or at risk of being infected with the SARS-CoV-2.

[0011] In another aspect, the present disclosure provides an isolated or recombinant antibody or an antigen-binding fragment thereof, which is capable of specifically binding to SARS-CoV-2, and exhibiting at least 50% less binding or non-detectable binding to SARS-CoV or MERS-CoV.

[0012] In another aspect, the present disclosure provides an isolated or recombinant antibody or an antigen-binding fragment thereof, having one or more features selected from the group consisting of: a) capable of specifically binding to spike protein of SARS-CoV-2 and exhibiting at least 50% less binding to spike protein of SARS-CoV or spike protein of MERS-CoV; b) capable of specifically binding to receptor-binding domain (RBD) of the spike protein of SARS-CoV-2 comprising the amino acid sequence of SEQ ID NO: 128; c) exhibiting binding to RBD of spike protein of SARS-CoV comprising the amino acid sequence of SEQ ID NO: 124 at a level that is non-detectable or that is no more than 50% of the binding to the RBD of spike protein of SARS-CoV-2; d) exhibiting binding to RBD of spike protein of MERS-CoV comprising the amino acid sequence of SEQ ID NO: 126 at a level that is non-detectable or that is no more than 50% of the binding to RBD of the spike protein of SARS-CoV-2; e) capable of binding to the RBD of spike protein of SARS-CoV-2 at a K_d value of no more than 1×10^{-7}M as measured by Surface Plasmon resonance (SPR); f) exhibiting binding to the RBD of spike protein of SARS-CoV or the RBD of spike protein of MERS-CoV at